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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,475	08/12/2002	Joshua W Hamilton.	DC-0190	1040

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EXAMINER
MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,475	HAMILTON ET AL.	
	Examin r	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *1-8, 10-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *03282002* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group VI in the reply filed 11/14/2003 is acknowledged. The traversal is on the ground(s) that the claims all relate to genetic constructs and methods for using those constructs to identify and assess the ability of anti-neoplastic agents to induce drug resistance, thus sharing the same inventive concept, and that there is a special technical relationship between Group I (drawn to a genetic construct comprising CFTR and eGFP) and Group VI (drawn to a method for identifying an agent). This is not found persuasive because the invention of Group I is separate and distinct from the invention of Group VI because the invention of Group I may be used in other methods than those of Group VI, such as in the production of the protein of interest (CFTR), thus they do not share a single inventive concept. Additionally, the special technical feature is not an advance over the prior art as demonstrated in the rejection under 35 USC § 103, *infra*.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

Claim 9 is objected to because of the following informalities: Claim 9 is dependent on a non-elected claims. Claim 9 is directed to methods using polynucleotides as set forth in non-elected claim 4. Appropriate correction is required.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying agents which increase functional cell surface expression of the deltaF508 CFTR protein by exposing cells comprising a genetic construct comprising human CFTR coding sequence and an eGFP reporter gene to the agent, measuring expression levels or trafficking of CFTR to the membrane, and comparing the levels of CFTR expression or tracking to controls, does not reasonably provide enablement for a method for identifying agents for use in the treatment of cystic fibrosis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue.

In the instant case, the claims are directed to a method for identifying agents for use in the treatment of cystic fibrosis. However, the method steps are directed to identifying an agent which increases expression or trafficking of CFTR to the cell membrane, and these are not the only deficiencies which lead to the CF phenotype. Mickle et al. teaches that the consequences of mutations in CFTR are grouped in to classifications, including synthesis, maturation and trafficking, activation, altered conductance, altered abundance, and the loss of regulatory activity (see Table 1, page 600). Since the claims are directed to methods for identifying compounds that

treat CF, the identified compound would need to function as a treatment in all these classes of disorder, while the methods will only identify compounds which affect expression or trafficking. Thus the claims are not enabled to the full scope. In addition, while the claims are directed to a method for identifying agents for use in the treatment of cystic fibrosis, the art recognizes that drugs which affect trafficking are not necessarily a treatment for CF since there is no clinically effective drug available for treatment of CF (Roomans GM. Pharmacological treatment of the ion transport defect in cystic fibrosis. Expert Opin Investig Drugs. 2001 Jan; 10(1): 1-19, at 1, column 1, third paragraph) despite the fact that compounds identified as affecting trafficking of CFTR to the cell membrane (i.e. 4PBA) are already known (Roomans at 6, column 1). Thus, since the claims as written encompass methods which identify only compounds which affect trafficking or expression of CFTR, but not the other manifestations of the CF phenotype, while additionally the art recognizes that there are currently no known pharmacological agents which treat CF, despite known agents which affect trafficking of CFTR, it would require undue experimentation to practice the method as claimed. It would require undue experimentation to practice the method as claimed because the skilled artisan would need to develop other methods that could identify an agent which would be efficacious in treating all forms of CF. Thus, due to the large quantity of experimentation necessary to practice the method as recited in the claim, the lack of direction/guidance presented in the specification regarding the methods which would identify compounds to treat all forms of CF, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of identifying compounds which can treat CF, and the breadth of the claims which encompass identification of compounds top treat any of the CF phenotypes, undue

experimentation would be required of the skilled artisan to practice the claimed invention in its full scope.

Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are directed to a method for identifying agents for use in the treatment of cystic fibrosis, thus encompassing a genus of methods given the diverse nature of the CF phenotype (see *supra*). However, the method steps are directed to identifying an agent which increases expression or trafficking of CFTR to the cell membrane, and these are not the only deficiencies which lead to the CF phenotype. Applicant has only taught methods to identify compounds that increase expression or trafficking of CFTR to the cell membrane using eGFP as a reporter. Thus, the scope of the claim includes numerous other methods, and the genus is highly variant because a significant number of differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the

genus is highly variant one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is vague and indefinite in that it is drawn to methods of identifying agents which are useful in the treatment of CF, because it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moyer et al. (1999) in view of Cormack et al. (1996).

Moyer (Moyer BD, Loffing-Cueni D, Loffing J, Reynolds D, Stanton BA. Butyrate increases apical membrane CFTR but reduces chloride secretion in MDCK cells. Am J Physiol. 1999 Aug; 277(2 Pt 2): F271-6) teaches a method of measuring the effect of butyrate on the expression of a CFTR-GFP nucleic acid. The construct comprising CFTR-GFP is set forth on page F272, column 2, third paragraph. The method is set forth on page F274 Figure 3. Moyer et al. does not teach the method using a nucleic acid construct comprising CFTR and eGFP.

Cormack et al. (Cormack BP, Valdivia RH, Falkow S. FACS-optimized mutants of the green fluorescent protein (GFP). Gene. 1996; 173(1 Spec No): 33-8) teaches the cloning of GFP mutants which fluoresce more intensely than wild type GFP (page 35, Figure 2). Therefore, it would have been obvious to one of skill in the art at the time the invention was made to practice a method for identifying agents which increase functional cell surface expression of the deltaF508 CFTR protein by exposing cells comprising a genetic construct comprising human CFTR coding sequence and an reporter gene to the agent, measuring expression levels or trafficking of CFTR to the membrane, and comparing the levels of CFTR expression or tracking to controls as taught in the Moyer reference, wherein the reporter gene is eGFP as taught in the Cormack reference. The motivation is provided in the Cormack reference that teaches that eGFP has a greatly increased fluorescence intensity, making the mutants useful for a number of applications (page 37, column 2, second paragraph).

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
January 21, 2004